CLAIMS

1. A single nucleotide polymorphism (SNP) representing the common DNA variant in humans providing a valuable resource for the genetic analysis of cancer, wherein the SNP resides in the carboxy terminal domain of $p21^{waf1/cip1}$ gene, encoding the PCNA binding motif, in the codon 149 (GAT→ GGT) of wild type $p21^{waf1/cip1}$ where the codon 149, GAT→GGT transition, is manifested as an amino acid substitution of *Aspartate* to *Glycine*.

2. A method for screening of subjects having or at risk of having esophageal cancer, the method comprising:
   a) amplifying a target nucleic acid in DNA isolated from a specimen of a subject;
   b) purifying the PCR products;
   c) DNA sequencing of the PCR products;
   d) detecting single nucleotide polymorphism in $p21^{waf1/cip1}$ gene by determining codon 149, GAT→GGT transition, or by observing the presence or absence of the codon 149 polymorphic variant, wherein the presence of the polymorphism is indicative of risk of cancer.

3. A method as claimed in claim 2, wherein in the target nucleic acid is DNA.

4. A method as claimed in claim 2, wherein the reagents are oligonucleotides.

5. A method as claimed in claim 2, wherein the target nucleic acid is amplified prior to detection.

6. A method as claimed in claim 2, wherein the amplification is effected by polymerase chain reaction (PCR) using specific oligonucleotide primers.

7. A method as claimed in claim 2, wherein the specimen comprises test sample selected from the group consisting of blood, normal tissue and tumor tissue.

8. A method as claimed in claim 2, wherein detection of $p21^{waf1/cip1}$ variant comprises:
   (a) determining the amino acid sequence of the $p21^{waf1/cip1}$ variant protein; and

(b) comparing the amino acid sequence of the p21$^{waf1/cip1}$ variant protein with the wild type p21$^{waf1/cip1}$ protein and identifying the alteration in the amino acid.

9. A method for designing and prescreening therapeutic agents for cancer treatments using p21$^{waf1/cip1}$ (condons 141-160) variant peptides to modify p21$^{waf1/cip1}$ PCNA interaction, said method comprising:

(a) using competitive PCNA-p21 peptides (141-160) binding assay for screening compounds that are capable of modulating PCNA-p21$^{waf1/cip1}$ interaction; and

(b) using this assay, rationally designed peptides for binding to PCNA and interruption of PCNA-p21 (141-160) complex.

10. A method of screening therapeutic agents for use in regulating the growth of cells by regulating the expression of variant or wild type, p21$^{waf1/cip1}$, said method comprising:

a) measuring in the presence of test substance binding of a protein/peptide which specifically binds to the variant p21$^{waf1/cip1}$ PCNA binding region to a DNA molecular sequence selected from the group consisting of nucleotides 141-160;

b) measuring the binding of said protein/peptide to said DNA molecular sequence in the absence of a test substance; and

c) comparing the measured binding of said protein/peptide in the presence of said test substance to the measured binding of said protein/peptide in the absence of said test substance, a test substance which increases or decreases the amount of binding being a candidate for use in regulating the growth of cells.

11. A method for screening therapeutic agents *in vitro* for use in regulating the expression of variant or wild type p21$^{waf1/cip1}$, said method comprising:

a) measuring *in vitro* transcription from a transcription construct, said transcription construct comprising a reporter gene which encodes an assayable product and a p21$^{waf1/cip1}$ PCNA binding sequence selected from the group consisting of nucleotides 144-151, said sequence being upstream from and adjacent to said reporter gene, said *in vitro* transcription being effected in the presence or absence of a test substance;

b) determining whether transcription of said reporter gene is altered by the presence of the test substance, which alters the transcription of said reporter gene being a candidate for use in regulating the growth of cells; and designing potential therapeutic agents (drugs, antisense oligonucleotides, etc.).

12. A method for identifying potential drug targets using a variant of PCNA binding motif of $p21^{waf1/cip1}$, said method comprising:

a) incubating a potential therapeutic agent with a cell which contains a reporter construct, cDNA fragment comprising the variant $p21^{waf1/cip1}$-PCNA binding region covalently linked in a cis configuration to a gene encoding an assayable product;

b) measuring the production of the assayable product;

c) identifying a potential therapeutic agent which decreases or increases the production by the cell of the assayable product;

d) using the absence of agent which supresses the growth of tumor cells by activating or inhibiting the expression of variant p21; and

e) using the association between SNP at codon 149 in $p21^{waf1/cip1}$ gene and esophageal SCCs as well as oral SCCs for assessing predisposition to other human cancers.

13. A method for genotyping cancer patients for $p21^{waf1/cip1}$ codon 149 variant as a predictor of radiosensitivity of tumors, said method comprising:

a) amplifying a target nucleic acid in DNA isolated from a specimen of a subject by polymerase chain reaction (PCR) using specific oligonucleotide primers;

b) purifying the PCR products;

c) DNA sequencing of the PCR products; and

d) detecting single nucleotide polymorphism in $p21^{waf1/cip1}$ gene by determining codon 149, GAT→GGT transition, or by observing the presence or absence of the codon 149 polymorphic variant, wherein the presence of the polymorphism is indicative of risk of cancer.

14. A method for genotyping cancer patients for p21$^{waf1/cip1}$ codon 149 variant using the method according to claim 2 for designing cancer treatment protocols.

15. A method according to claim 2, wherein the polymerase chain reaction (PCR) products are purified using agarose gels, and the DNA sequencing of the PCR products use both forward and reverse primers.

16. A method according to claim 13, wherein the polymerase chain reaction (PCR) products are purified using agarose gels, and the DNA sequencing of the PCR products use both forward and reverse primers.